

FIG. 1A

2nd Round: screening of mutants at (surrounding) HIT positions

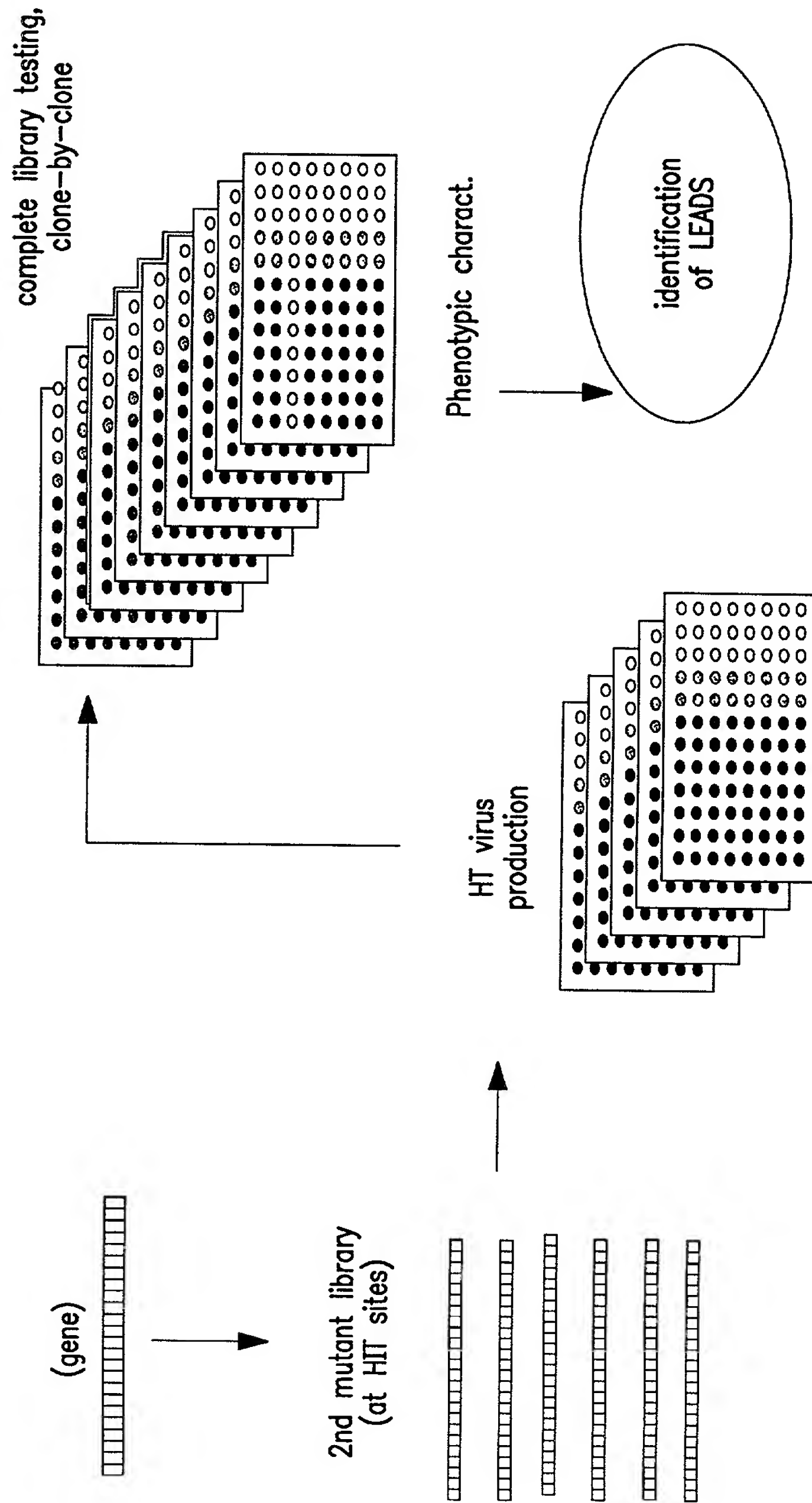


FIG. 1B

3rd Round: screening of recombinants between LEADS

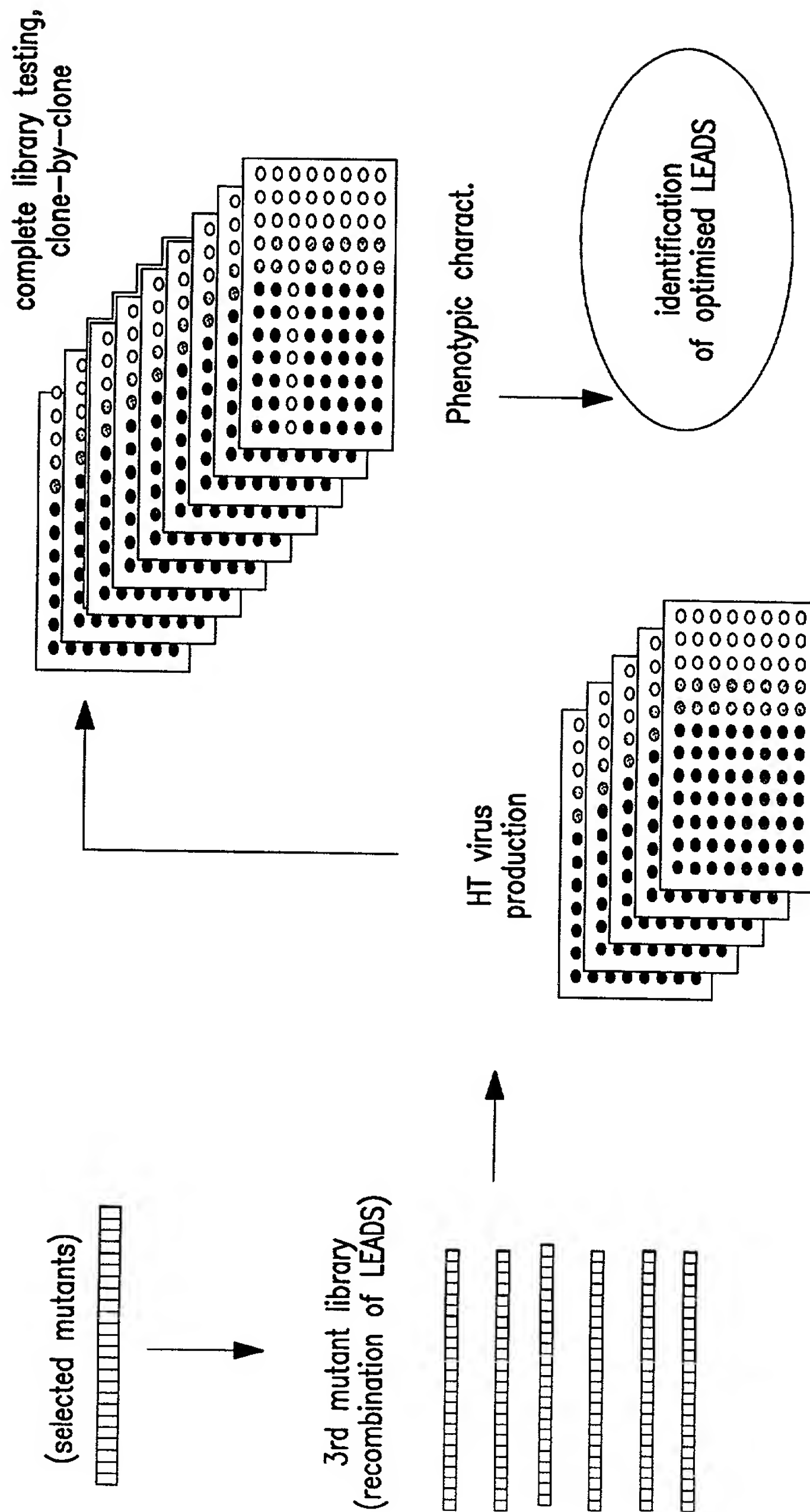


FIG. 1C

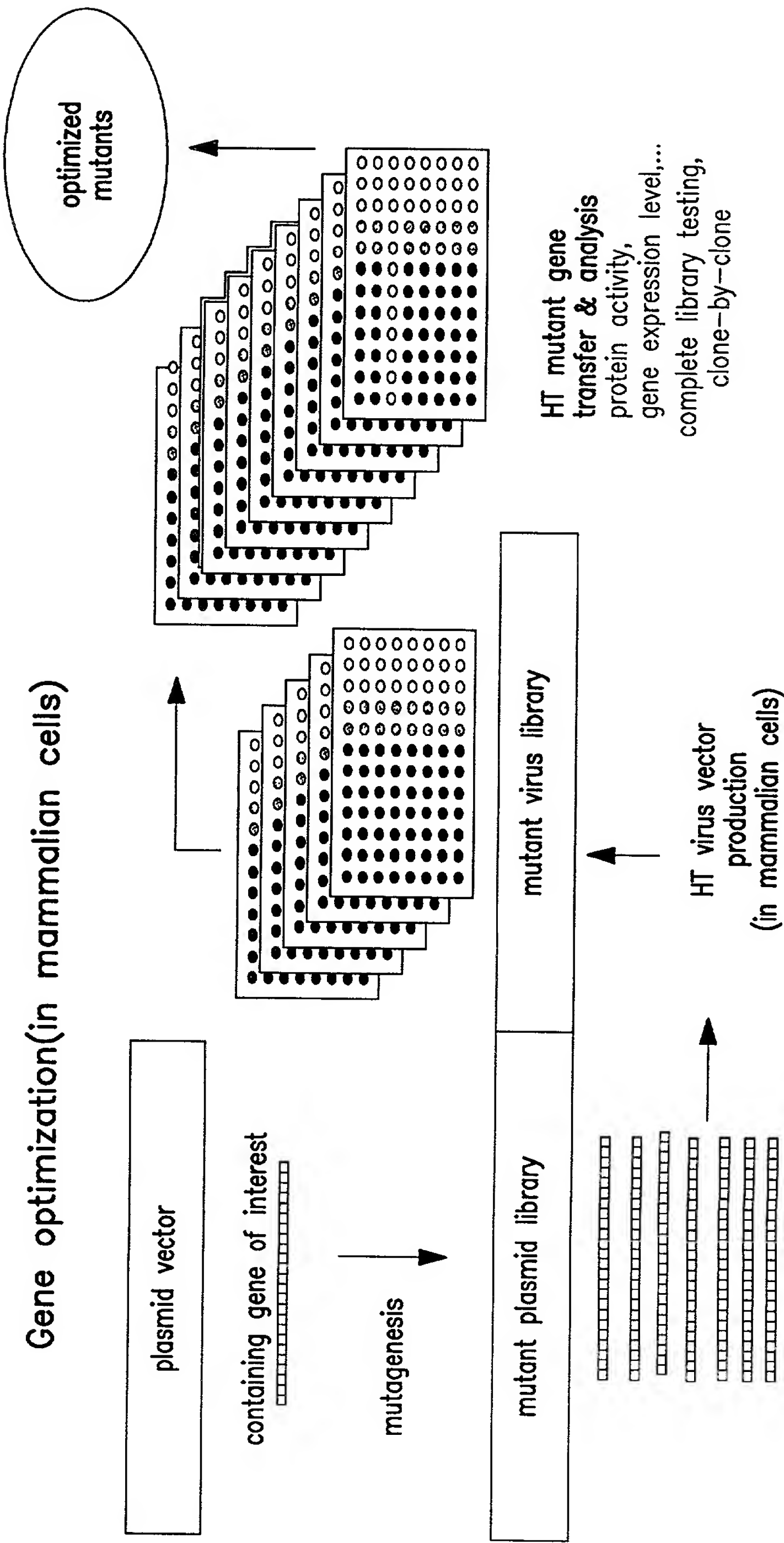


FIG. ID

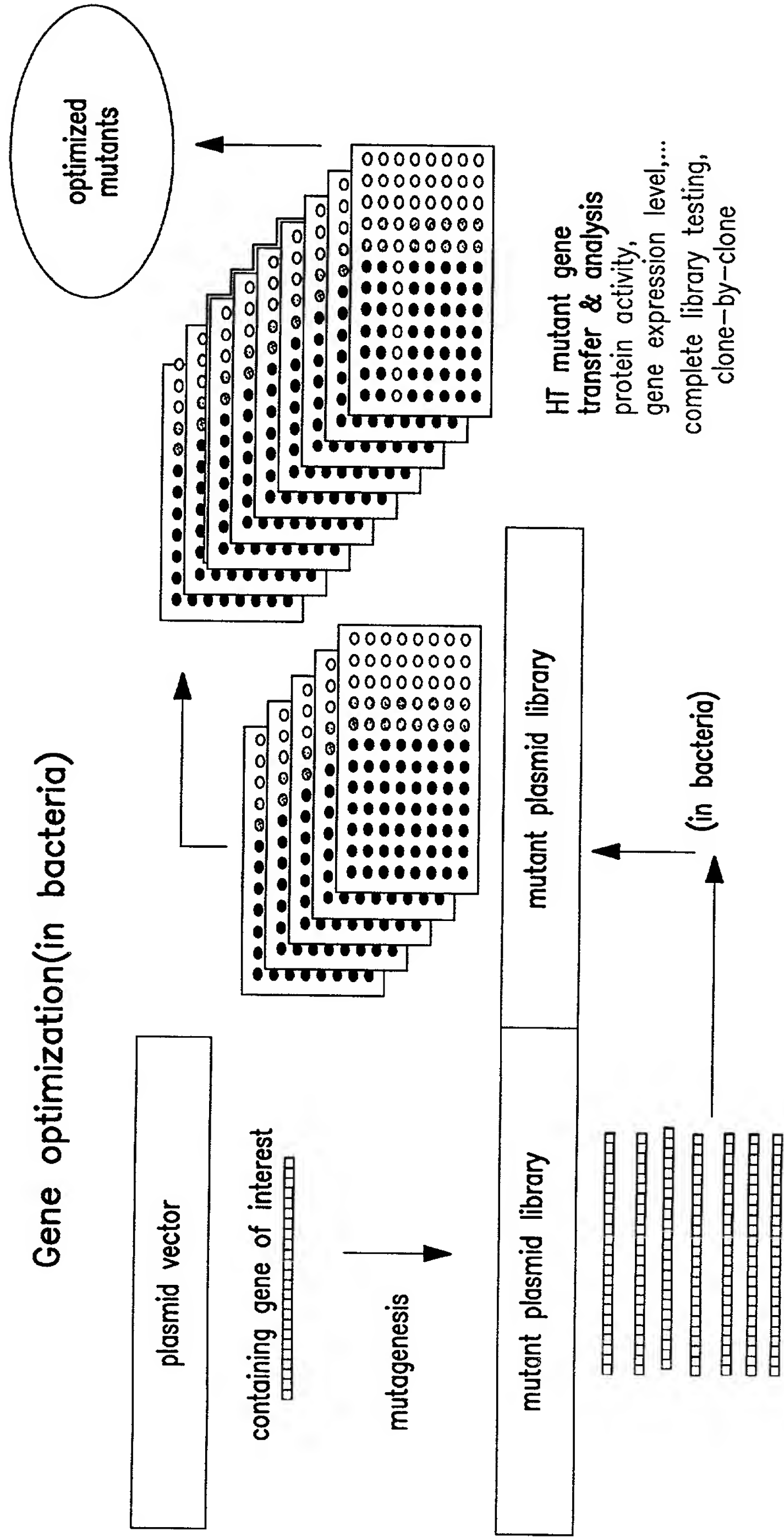


FIG. 1E

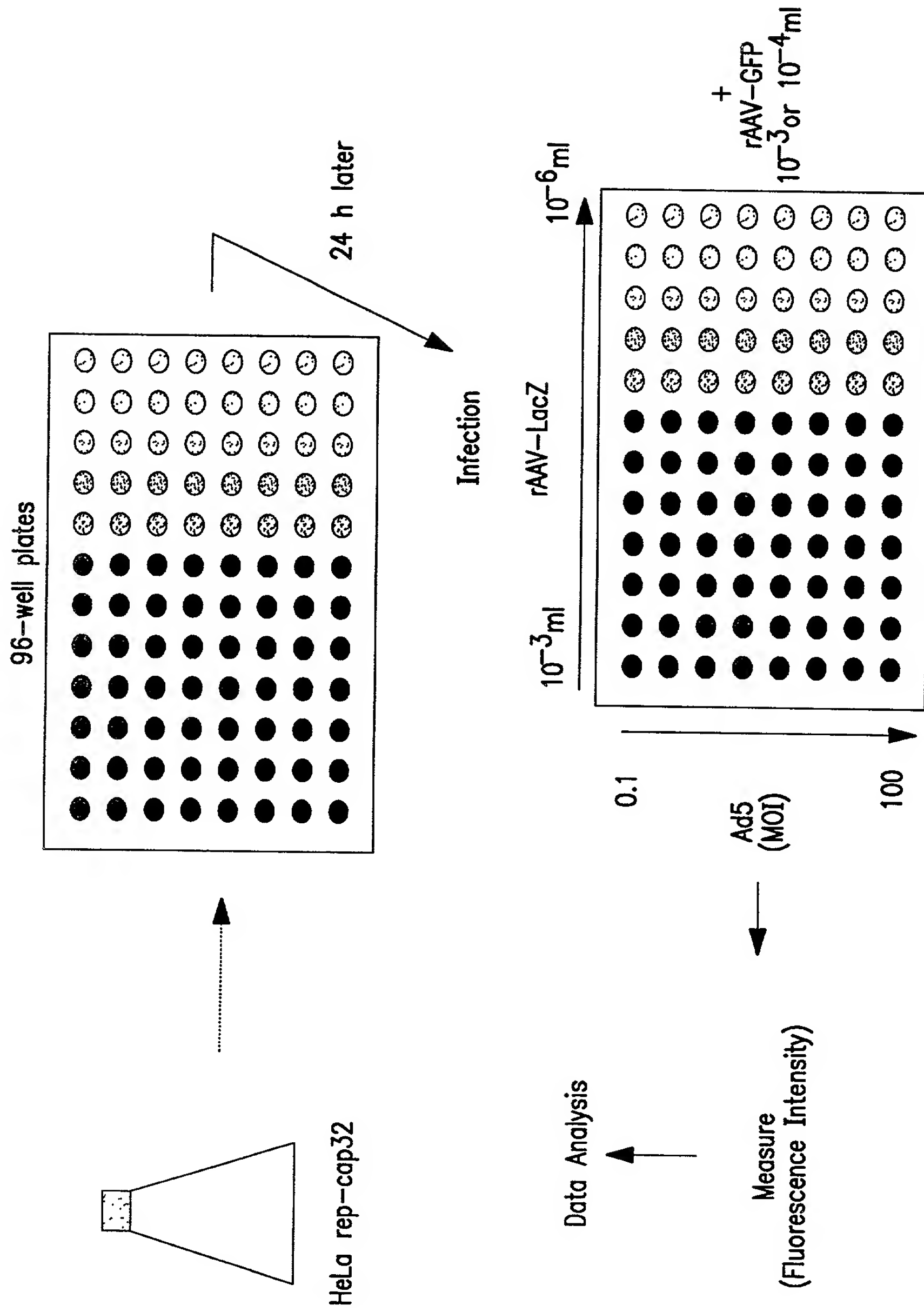


FIG. 2A

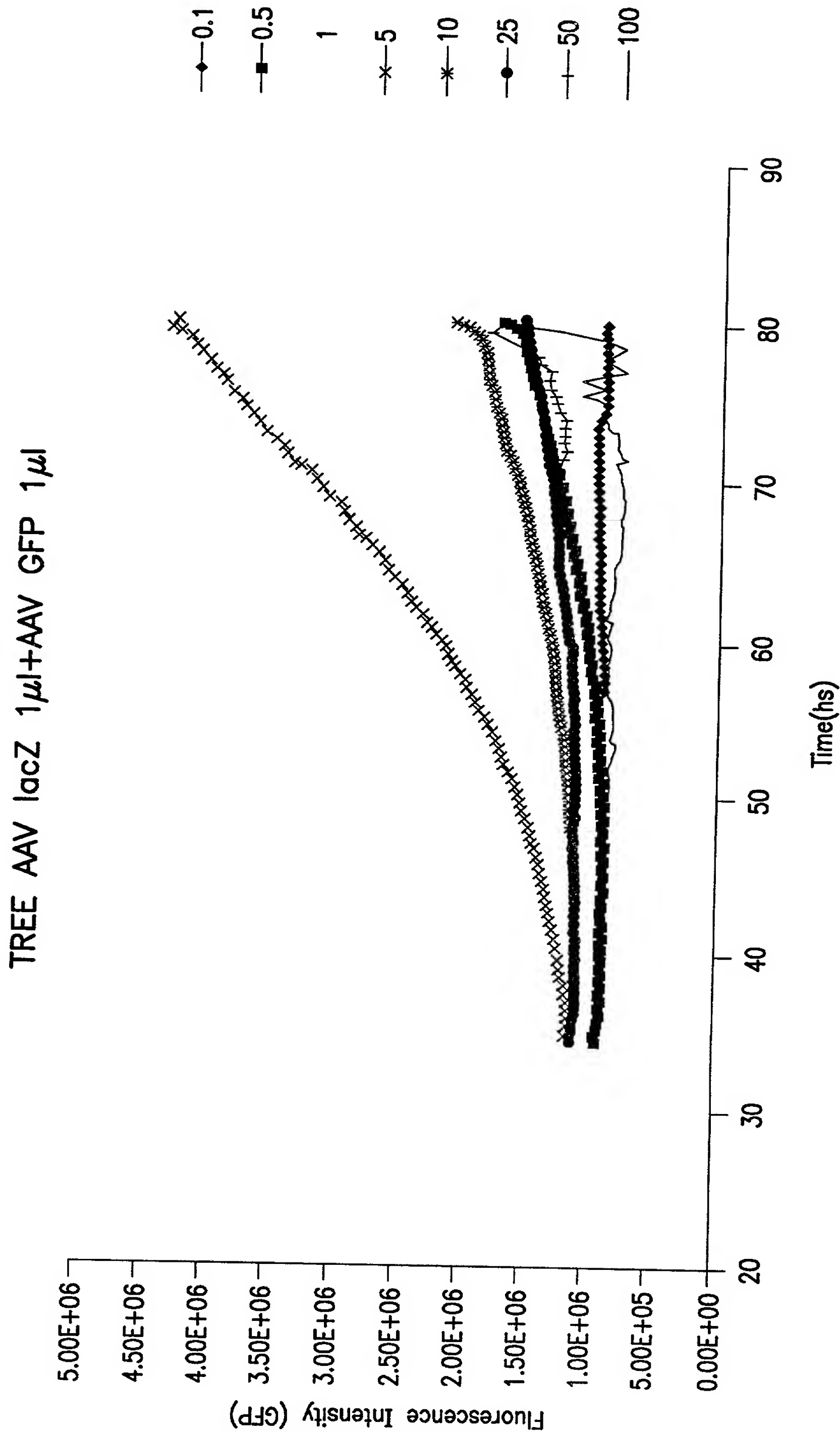


FIG. 2B

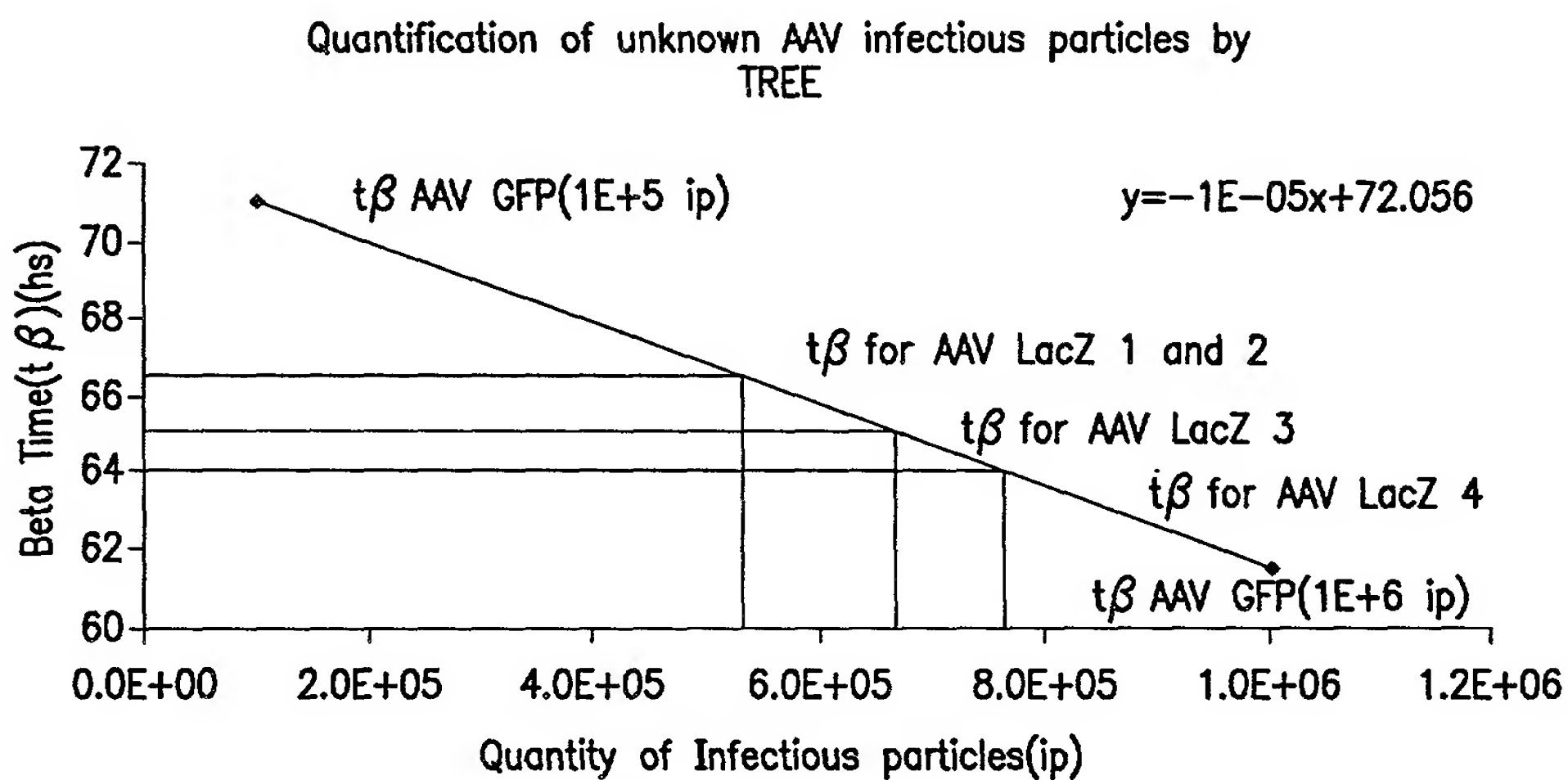


FIG. 2C

Hits on Rep

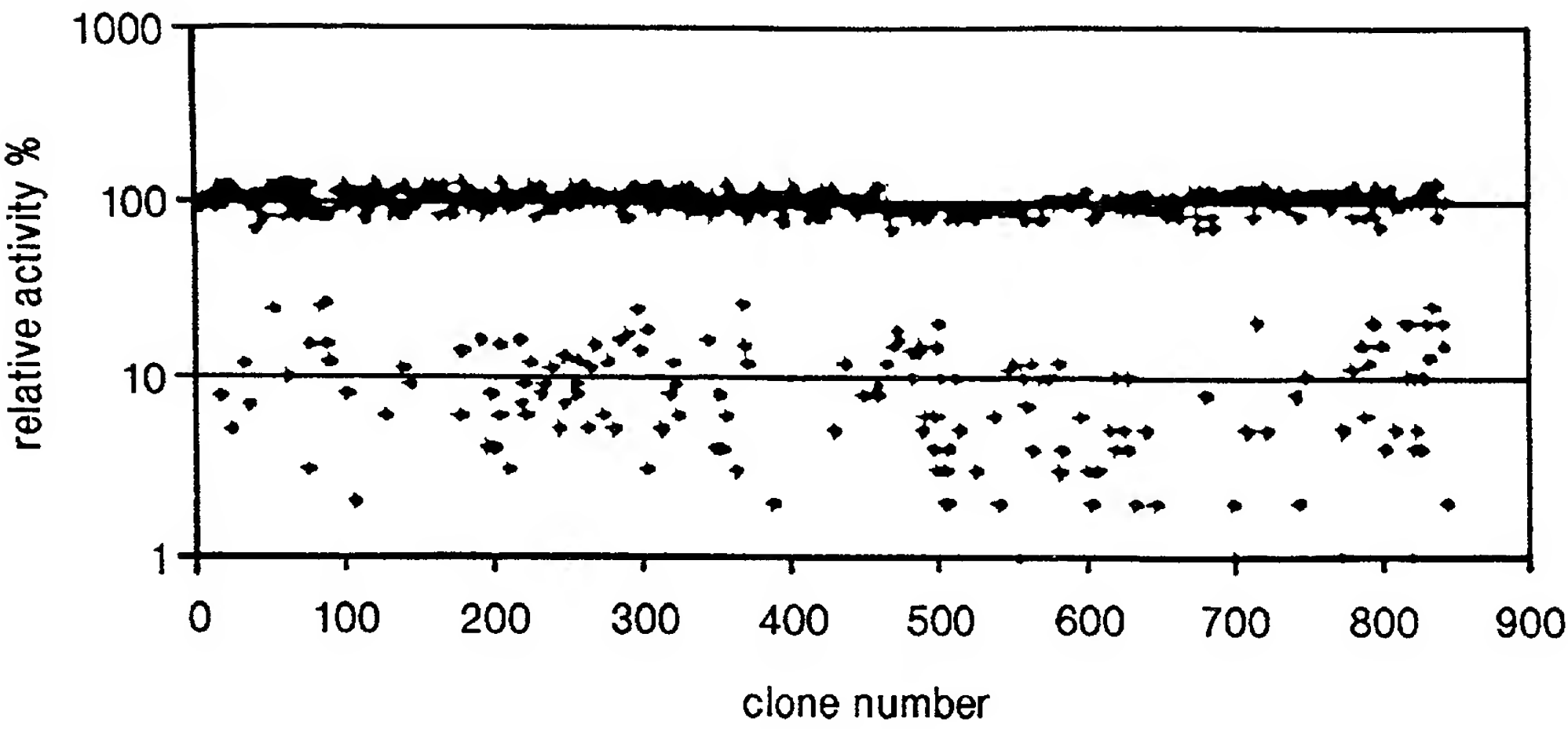


FIG. 3A

Lead positions on Rep

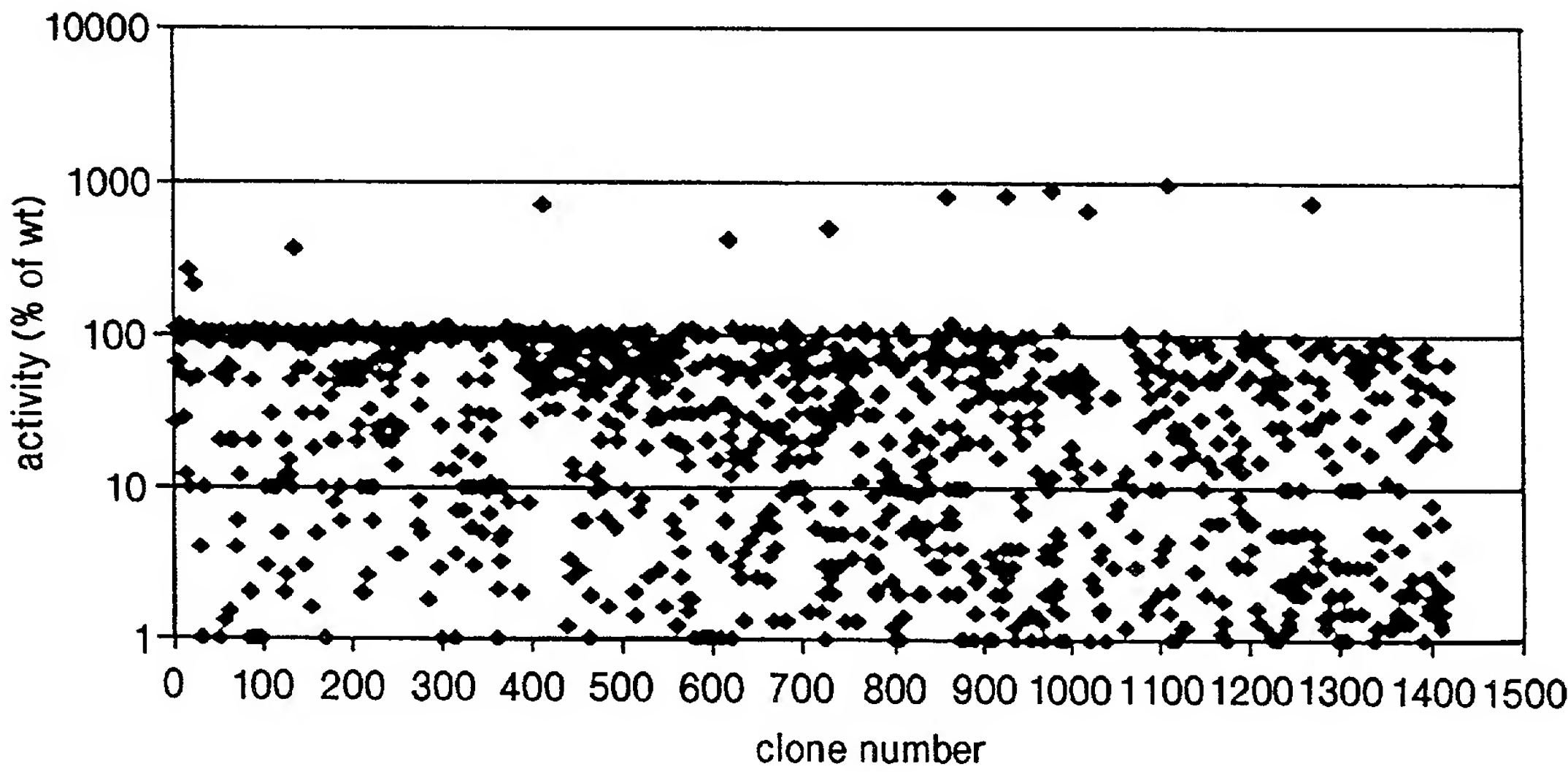


FIG. 3B

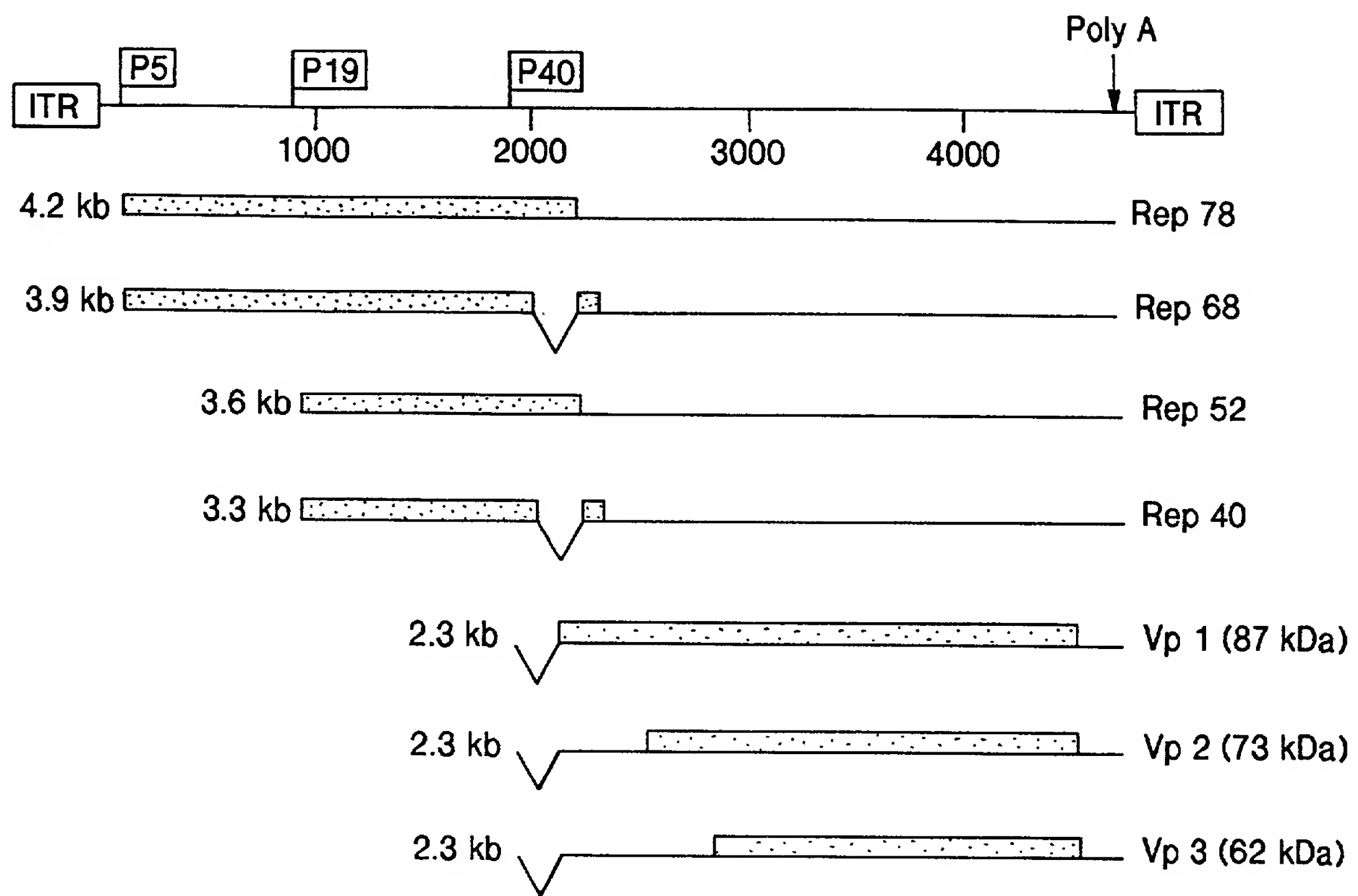


FIG. 4

```

      10      20      30      40      50      60
1  MPGFYEIVIKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSDMDLNLIEQAPLTVAEKLQ 60
2  MPGFYEIVIKVPSDLDEHLPGISDSFVNWVAEKEWELPPDSDMDLNLIEQAPLTVAEKLQ 60
3  MPGFYEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSDMDPNLIEQAPLTVAEKLQ 60
4  MPGFYEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSDMDPNLIEQAPLTVAEKLQ 60
5  MPGFYEIVLKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSDMDLNLIEQAPLTVAEKLQ 60
6  MPGFYEIVIKVPSDLDGHLPGISDSFVNWVAEKEWELPPDSDMDLNLIEQAPLTVAEKLQ 60
7  MATFYEIVIRVPFDVEEHLPGISDSFVDWVTGQIWELPPESDLNLTVEQPQLTVADRIR 60
C  M**FYE**:*VP*D***HLPGIS+SFV:WV****WELPP*SD**+*L*EQ**LTVA****
      70      80      90     100     110     120
1  RDFLVQWRRVSKAPEALFFVQFEKGESYFHLHLVETTGVKSMVLGRFLSQIRDKLVQTI 120
2  RDFLVQWRRVSKAPEALFFVQFEKGESYFHLHLVETTGVKSMVLGRFLSQIRDKLVQTI 120
3  REFLVEWRRVSKAPEALFFVQFEKGETYFHLHVLITIGVKSMVVGGRYVSQIKEKLVTRI 120
4  REFLVEWRRVSKAPEALFFVQFEKGETYFHLHVLITIGVKSMVVGGRYVSQIKEKLVTRI 120
5  REFLVEWRRVSKAPEALFFVQFEKGDYFHLHLVETVGVKSMVVGGRYVSQIKEKLVTRI 120
6  RDFLTEWRRVSKAPEALFFVQFEKGESYFHMHLVETTGVKSMVLGRFLSQIREKLIQRI 120
7  RVFLYEWNKFSKQ-ESKFFVQFEKGESEYFHLHTLVETSGISSMVLGRYVSQIRACLKVV 119
C  R:FL++W***SK**E**FFVQFEKG+:YFH*H:L+ET:G**SMV:GR::SQI::*L*::*

      130     140     150     160     170     180
1  YRGIEPTLPNWFVAVTKTRNGAGGGNKVVDECIIPNYLLPKTQPELQWAWTNMEEYISACL 180
2  YRGIEPTLPNWFVAVTKTRNGAGGGNKVVDECIIPNYLLPKTQPELQWAWTNMEEYISACL 180
3  YRGVEPQLPNWFVAVTKTRNGAGGGNKVVDDCIIPNYLLPKTQPELQWAWTNMDQYLSACL 180
4  YRGVEPQLPNWFVAVTKTRNGAGGGNKVVDDCIIPNYLLPKTQPELQWAWTNMDQYLSACL 180
5  YRGVEPQLPNWFVAVTKTRNGAGGGNKVVDDCIIPNYLLPKTQPELQWAWTNMDQYISACL 180
6  YRGIEPTLPNWFVAVTKTRNGAGGGNKVVDECIIPNYLLPKTQPELQWAWTNMEQYLSACL 180
7  FQGIPEQINDWVAITKVKK--GGANKVVDSGYIPAYLLPKVQPELQWAWTNLDEYKLAAL 177
C  **G:EP:***W*A*TK*****GG*NKVVD:*YIP*YLLPK*QPELQWAWTN*:Y:*A*L

      190     200     210     220     230     240
1  NLAERKRLVAQHLTHVSQTQEONKENLNPNNSDAPVIRSKTSARYMELVGWLVDRGITSEK 240
2  NLAERKRLVAHDLTHVSQTQEONKENLNPNNSDAPVIRSKTSARYMELVGWLVDRGITSEK 240
3  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK 240
4  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK 240
5  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK 240
6  NLTERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDKGITSEK 240
7  NLEERKRLVAQFLAESSQRS-QEAASQREFSADPVIKSKTSQKYMALVNWLVVEHGITSEK 236
C  NL+ERKRLVA*+L***SQ***Q*****S**PVI*SKTS**YM*LV*WLV*+GITSEK

      250     260     270     280     290     300
1  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMALTKSAPDYLVGPPADIKTNRIYR 300
2  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMALTKSAPDYLVGPPADIKTNRIYR 300
3  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGSNPPEDITKNRIYQ 300
4  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGSNPPEDITKNRIYQ 300
5  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGQNPPEDISSNRIYR 300
6  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMSLTKTAPDYLVGQOPVEDISSNRIYK 300
7  QWIQENQESYLSFNSTGNSRSQIKAALDNATKIMSLTKSAVDYLVGSSVPEDISKNIWQ 296
C  QWIQE*Q*SY*SFN***NSRSQIKAALDNA:KIM+LTK:A*DYLVG::**+DI::NRI*:

      310     320     330     340     350     360
1  ILELNGYEPAYAGSVFLGWAQKRFGRNTIWLFGPATTGKTNIAEAIAHAVPFYGCNVWT 360
2  ILELNGYDPAYAGSVFLGWAQKRFGRNTIWLFGPATTGKTNIAEAIAHAVPFYGCNVWT 360
3  ILELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIAHAVPFYGCNVWT 360
4  ILELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIAHAVPFYGCNVWT 360
5  ILEMNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIAHAVPFYGCNVWT 360
6  ILELNGYDPQYAASVFLGWATKKFGKRNTIWLFGPATTGKTNIAEAIAHTVPFYGCNVWT 360
7  IFEMNGYDPAYAGSILYGWCQRSFNKRNTVWLYGPATTGKTNIAEAIAHTVPFYGCNVWT 356
C  I*E+NGY*P:YA:S***GW***:F*KRNT*WL*GPATTGKTNIAEAIAH+VPFYGCNVWT
```

FIG. 5A

```

      370      380      390      400      410      420
1  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
2  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
3  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIEPTPVIVTS 420
4  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIEPTPVIVTS 420
5  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
6  NENFPFND CVDKMVIWEEGKMTAKVVESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
7  NENFPFND CVDKMLIWEEGKMTNKVVESAKAILGGSKVRVDQKCKSSVQIDSTPVIVTS 416
C  NENFPFND CVDKM*IWEEGKMT*KVVESAKAILGGSKVRVDQKCKSS*QI+*TPVIVTS

      430      440      450      460      470      480
1  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKEFFRWAQDHSVTEV 480
2  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKEFFRWAQDHSVTEV 480
3  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTDV 480
4  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTDV 480
5  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTKRLEHDGKVTQKEVKDFFRWASDHVTEV 480
6  NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWAKDHSVVEV 480
7  NTNMC VVDGNSTTFEHQQPLEDRMFKFELTKRLPPDFGKITQKEVKDFFAWAKVNQVPV 476
C  NTNMC *V* DGNSTTFEHQQPL*DRMFKFELT+RL: *DFGK*TKQEVK+FF*WA: ****+:V

      490      500      510      520
1  AHEFYVRKGGANKRPAPDDADKSEPKRA-----CPSVADPSTSDAEG 522
2  AHEFYVRKGGANKRPAPDDADKSEPKRA-----CPSVADPSTSDAEG 522
3  AHEFYVRKGGAKKRPASNDADVSEPKRQ-----CTSLAQPTTSDAEA 522
4  AHEFYVRKGGAKKRPASNDADVSEPKRQ-----CTSLAQPTTSDAEA 522
5  THEFYVRKGGARKRPAPNDADISEPKRA-----CPSVAQPSTSDAEA 522
6  EHEFYVKKGGAKKRPAPSDADISEPKRV-----RESVAQPSTSDAEA 522
7  THEFKVPRELAGTKGAEKSLKRPLGDTVNTSYKSLEKRARLSFVPETPRSSDVTVDPAPL 536
C  :HEF*V+***A:***A:;***.*****; +:***:***A*:

      530      540      550      560      570      580
1  APVDFADRYQNKCSRHAGMLQMLFPCKTCERMNQNFNICFTHGTRDCSECFP--GVSESQ 580
2  APVDFADRYQNKCSRHAGMLQMLFPCKTCERMNQNFNICFTHGTRDCSECFP--GVSESQ 580
3  P-ADYADRYQNKCSRHVGMNLMLFPCKTCERMNQISNVCFTHGQRDCGECFPGMSESQPV 581
4  P-ADYADRYQNKCSRHVGMNLMLFPCKTCERMNQISNVCFTHGQRDCGECFPGMSESQPV 581
5  P-VDYADRYQNKCSRHVGMNLMLFPCRQCERMNQNVDFICFTHGVMDCAEFCF--VSESQPV 580
6  S-INYADRYQNKCSRHVGMNLMLFPCRQCERMNQNSNICFTHGQKDCLECFP--VSESQP 579
7  RPLNWNNSRYDCKCDYHAQFDNISNKCDECEYLNRGKNGCICHNVTHCQICHG----- 588
C  ::+:**RY**KC**H:**:****C::CE**N*:*:C**H*:*C.*C**...+:::

      590      600      610      620
1  PVVRKRRTYRKLCAIHHLLGRAPEIACSACDLVNVDLDDCVSEQ 623
2  PVVRKRRTYRKLCAIHHLLGRAPEIACSACDLVNVDLDDCVSEQ 623
3  SVVKKKTYQKLCPIHHILGRAPEIACSACDLANVDLDDCVSEQ 624
4  SVVKKKTYQKLCPIHHILGRAPEIACSACDLANVDLDDCVSEQ 624
5  SVVRKRRTYQKLCPIHHIMGRAPEVACSACELANVDLDDCDMEQ 623
6  VSVVKKAYQKLCYIHHIMG-KVPDACTACDLVNVDLDDCIFEQ 621
7  -----IPPWEKENLSDFGDFDDANKEQ 610
C  :+*:+:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*D*DD*: :EQ
```

FIG. 5B